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|   |                      |                        |          |
|---|----------------------|------------------------|----------|
| <b>TRANSMITTAL FORM</b><br><br>(to be used for all correspondence after initial filing) | Application Number   | 10/539,842             |          |
|   | Filing Date          | June 20, 2005          |          |
|   | First Named Inventor | MUNTAU-HEGER           |          |
|   | Art Unit             | 1614                   |          |
|   | Examiner Name        | VAKILI, Zohreh         |          |
| Total Number of Pages in This Submission  | 10                   | Attorney Docket Number | 3535.020 |

| ENCLOSURES (Check all that apply)   |   |  |
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| SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT |                           |          |        |
|--|---------------------------|----------|--------|
| Firm Name                                  | Akerman Senterfitt        |          |        |
| Signature                                  | <i>Nicholas J. Landau</i> |          |        |
| Printed name                               | Nicholas J. Landau, Ph.D. |          |        |
| Date                                       | 11/02/2006                | Reg. No. | 57,120 |

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| Typed or printed name   | Nicholas J. Landau, Ph.D. | Date | 11/02/2006 |

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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of MUNTAU-HEGER, *et al.*

Confirmation No. 5018

Application No. 10/539,842

Examiner: VAKILI, Zohreh

Filed: June 20, 2005

Group Art Unit: 1614

Attorney Docket No. 3535.020

For: USE OF TETRAHYDROBIOPTERINE DERIVATIVES IN THE TREATMENT  
AND NUTRITION OF PATIENTS WITH AMINO ACID METABOLIC DISORDERS

**INFORMATION DISCLOSURE STATEMENT**

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Nicholas J. Landau Reg. No. 57,120  
Nicholas J. Landau, Ph.D.

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Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

In accordance with the duty of disclosure under 37 C.F.R. §1.56, Applicants hereby notify the U.S. Patent Office of the documents which are listed on the attached Forms PTO/SB/08A and PTO/SB/08B.

Applicants submit that the present invention is patentable over the cited references and submission of the listed documents is not intended as an admission that such documents constitute prior art against the present application. Applicants do not waive any right to take any action that would be appropriate to antedate or otherwise remove the listed documents as competent references against the present application.

The below references 2, 3, 9, 12, 13, 19, 22, 28, 31, and 33 were cited in the European Search Report issued in corresponding European application as "Category X," or of particular relevance. The references 2, 3, 6, 13, 19, 21, and 30 were cited in a European Office Action for the corresponding International Application. References 1 – 5, 7, 8, 10, 11, 13 – 15, 17, 18, 20, 23 – 29, and 31 – 33 were cited in a Protest of the U.S. National Phase of International Application no. PCT/EP2003/014262 pursuant to 37 C.F.R. §1.291. Copies of U.S. references are not enclosed. A copy of each foreign language reference is enclosed, along with a English translation of the abstract, where available. A copy of the international search report and European Office Action (in German, as no English translation is available) are also enclosed.

Applicants respectfully request that the listed documents be considered by the Examiner and made of record in the present application and that an initialed copy of forms PTO/SB/08A and PTO/SB/08B be returned in accordance with MPEP §609.

1. U.S. Patent No. 4,774,244
2. U.S. Patent No. 4,778,794
3. U.S. Publication No. 2002/0052374 A1
4. U.S. Patent No. 5,763,392
5. U.S. Patent No. 6,428,990 B1
6. WO 1995/13803
7. BATES, et al., "Children's Medications: A Parent's Guide", page 6, Harvery Whitney Books, Cincinnati, Ohio, (1996).
8. BLAU, et al., "34th EMG Meeting, Zurich CH, held May 31-June 2, 2003", proceedings published October 2002.
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20. KURE, et al., Tetrahydrobiopterin-responsive phenylalanine hydroxylase deficiency", The Journal of Pediatrics, 135:375-8 (1999).
21. MILLER, et al., "Role of Hydroxylase Cofactor in Regulating Dopamine Synthesis: Relevance to Neurological Disorders", 471-474 (1986).
22. MUNTAU, et al., "Tetrahydrobiopterin as an Alternative Treatment for Mild Phenylketonuria", N Engl J Med, 347-26:2122-32 (2002).

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25. "PhenylAde", Product Guide, Applided Nutrition Corp., (May 2002).
26. SCHAUB, et al., "Tetrahydrobiopterin therapy of atypical phenylketonuria due to defective dihydrobiopterin biosynthesis", *Archives of Disease in Childhood*, 53:674-683 (1978).
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30. TANAKA, et al., "On-off phenomenon in a child with Tetrahydrobiopterin deficiency due to 6-pyruvoyl tetrahydropterin synthase...", *Eur J Pediatr*, 148:450-52 (1989).
31. TREFZ, et al., "Successful treatment of phenylketonuria with tetrahydrobiopterin", *Eur J. Pediatr*, 160:315 (2001).
32. WALTER, et al., "Inhalation of the Nitric Oxide Synthase Cofactor Tetrahydrobiopterin in Health Volunteers", *Am J Respir Crit Care Med*, 156: 2008-10 (1997).
33. WEGLAGE, et al., "Tetrahydrobiopterin responsiveness in a large series of phenylketonuria patients", *J. Inherit. Metab. Dis.* 25:321-322 (2002).

Certification

This Statement is being filed prior to the issuance of the first Office Action for the present application, and this paper is thus submitted in accordance with 37 C.F.R. 1.97(b).

In view of the above certification, a fee is not required for consideration of this document. Nevertheless, should a fee be deemed to be due by the Commissioner, such fee should be charged to Deposit Account No. 50-0951.

Respectfully submitted,

Dated: 11/02/2006

Nicholas J. Landau  
Nicholas J. Landau, Ph.D.  
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Docket No. 3535.020

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| Sheet | 1 | of | 4 |
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|------------------------|----------------|
| Application Number     | 10/539,842     |
| Filing Date            | June 20, 2005  |
| First Named Inventor   | MUNTAU-HEGER   |
| Art Unit               | 1614           |
| Examiner Name          | VAKILI, Zohreh |
| Attorney Docket Number | 3535.020       |

## U. S. PATENT DOCUMENTS

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**FOREIGN PATENT DOCUMENTS**

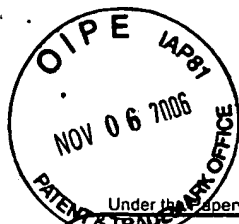
| Examiner Initials* | Cite No. <sup>1</sup> | Foreign Patent Document   | Publication Date | Name of Patentee or Applicant of Cited Document | Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear | T <sup>6</sup> |
|--------------------|-----------------------|---|------------------|---|---|----------------|
|                    |                       | Country Code <sup>3</sup> -Number <sup>4</sup> -Kind Code <sup>5</sup> (if known) | MM-DD-YYYY       |   |   |                |
|                    |                       | WO 1995/13803   | 05-26-1995       | CORNELL RESEARCH                                |   |                |
|                    |                       |   |                  |   |   |                |
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| Examiner<br>Signature |  | Date<br>Considered |  |
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| Examiner Name          | VAKILI, Zohreh |
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Sheet 2 of 4

### NON PATENT LITERATURE DOCUMENTS

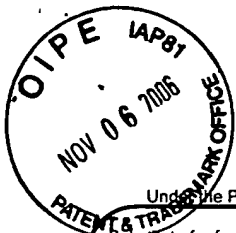
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|                    |                       | BATES, et al., "Children's Medications: A Parent's Guide", page 6, Harvery Whitney Books, Cincinnati, Ohio, (1996).   |                |
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| <b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br><br>(Use as many sheets as necessary) | <b>Application Number</b>     |    | 10/539,842     |
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|   | <b>Examiner Name</b>          |    | VAKILI, Zohreh |
|   | <b>Attorney Docket Number</b> |    | 3535.020       |
| Sheet   | 3                             | of | 4              |

**NON PATENT LITERATURE DOCUMENTS**

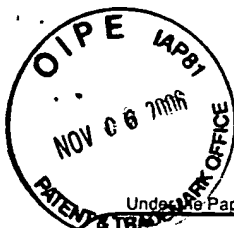
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Sheet 4 of 4

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| Examiner<br>Initials* | Cite<br>No. <sup>1</sup> | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. | T <sup>2</sup> |
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\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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